Health Effects of Airborne Particulate Matter

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What Do We Know: 1993-2006

- Human studies observed strong association between premature death and long term residence in areas with high PM concentrations
- The deaths appear due to cardiopulmonary causes
- Similar associations have been observed with asthma exacerbations and aggravation of other respiratory diseases
- Proximity to busy roads, with a high density of diesel vehicles, increases the risk of negative health effects
- State of California has declared diesel particulate a human lung carcinogen

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Summary of PM Center Findings

- A wider range of target tissues and health endpoints are associated with PM exposure than was known in 1997
- Mobile sources are highly relevant to the risks posed by ambient PM
- Improved mechanistic understanding of PM toxicity

Ultrafine particles have an important role in toxicity

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Health Effects Associated with PM Exposure

- CNS and autonomic nervous system
- Development: Low birth weight/preterm birth
- Increase in asthma and other respiratory disease in children
- Decrease in lung development and function in children
- Cardiovascular disease including atherosclerosis in adults
- Cancer

All Airborne PM is toxic to some degree; potency is based on physical and chemical characteristics

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Airborne Particulate Matter (PM) and Health Effects

For each 10 µg/m^3 increase in PM:

- Cardiopulmonary 6% increase in mortality
- Lung cancer 8% increase in mortality

We generally talk about three size ranges, coarse, fine and ultrafine

- Coarse – 2.5 to 10 µ m
- Fine – Less than 2.5 µ m
- Ultrafine – Less than 0.1 µ m

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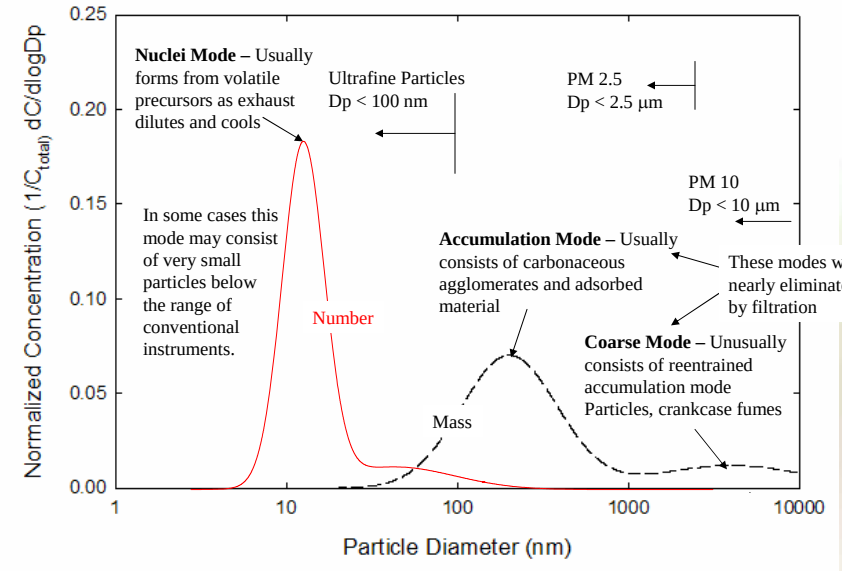
Typical Diesel Particle Size Distributions, Mass and Number Weighted



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Diesel Ultrafine PM

- Particles are in the emissions from fossil fuel combustion
- Particles can be formed AFTER emissions are exhausted when hot exhaust hits cool air and vapors condense/nucleate to form particles
- These latter particles are especially important because they are not eliminated by particle traps that will be required in 2007
- They are the basis for the high number concentrations near freeways

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Particle Counts in the LA Basin

	Particles/cc*
• Coastal air	600
• San Pedro	42,000
• 110 freeway (no diesel)	135,000
• 710 freeway (Long Beach)	300-600,000
• 710 freeway (max)	up to 1.5 million

**cc is the size of a sugar cube*

Source: Dane Westerdahl, ARB and Southern California Particle Center

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Tunnel Studies: PM Mass Decreases; Particle Number Increases Over Time

	Kirchstetter Study (1997)	PM Center (2004)
Bore 1 (Mixed HDV,LDV		
PM10 (μ g/m3)	130.0	37.2
PM2.5 (μ g/m3)	115.7	36.7
Number (particles/cm3)	340,000	550,000
Bore 2 (LDV only)		
PM10 (μ g/m3)	40.0	19.4
PM2.5 (μ g/m3)	40.9	15.3
Number (particles/cm3)	185,000	450,000

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Model for the Formation of Airborne Particulate Matter

- Particles generated during combustion of organics will become rapidly coated with gas-phase adsorbates strongly retained by the surface
- Ultrastructural analysis of lung tissue found that inhaled ultrafine particles were located within and beyond the epithelial barrier, in the main lung tissue compartments, cytoplasm and the nucleus of cells
- Particles within cells are not membrane bound and have direct access to intracellular proteins, organelles, and DNA which may greatly enhance their toxic potential
- The toxic potential of UFPs is greatly enhanced by their free location and movement within cells

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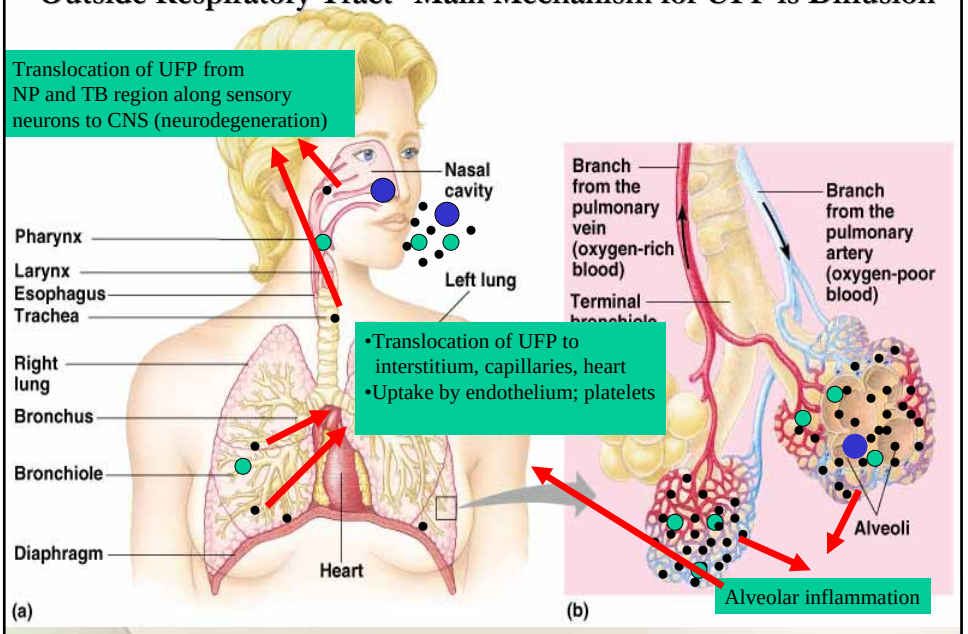
Deposition and Pathways of Particle Translocation Within and Outside Respiratory Tract--Main Mechanism for UFP is Diffusion



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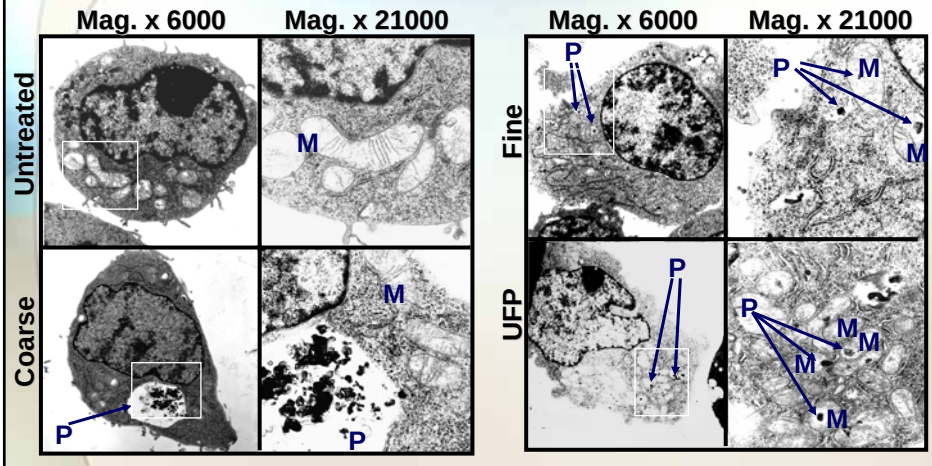
Mitochondria: An Important Subcellular Target of PM and a Source of ROS Generation



Mitochondria are redox active organelles

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Source: Li, et al, 2003

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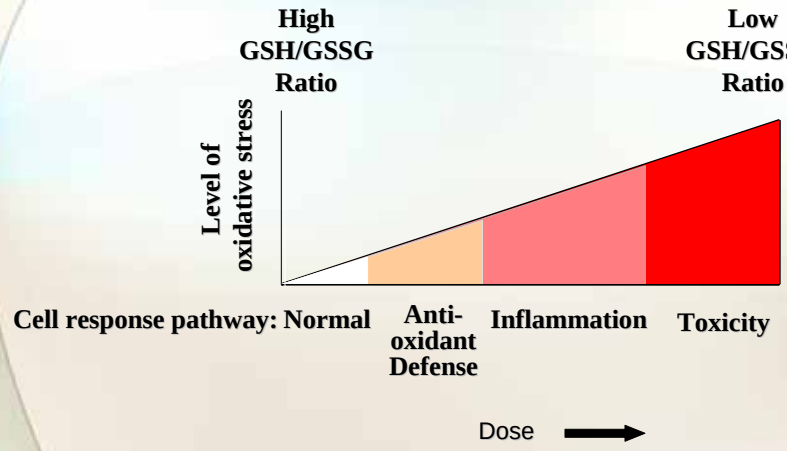
Pathways of Oxidative Stress



Source: Xiao, et al. 2003

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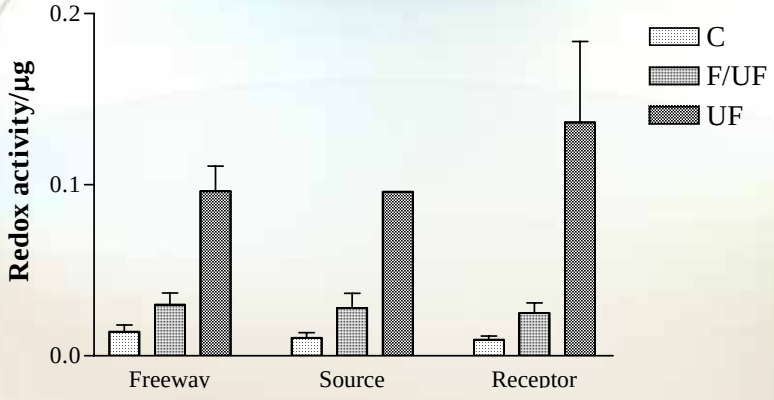
Redox Activity



When activity is expressed per mass, the results reflect the potency of the sample

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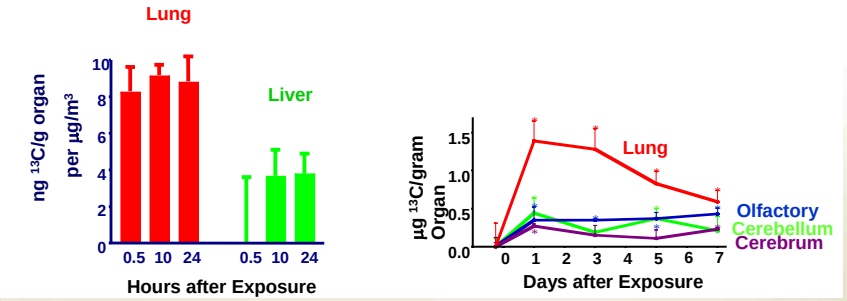
Does PM Affect Other Organ Systems?

Labeled ultrafine particles are translocated to the lung and to specific regions of the brain, where they stimulate brains cells to produce pro-inflammatory markers: the particles appear to be preferentially located in the mitochondria: redox active



Brain Inflammation Markers Tissue from Mice Exposed at BH2 2002			
	Control	UF	F+UF
TNFα (ng/mL)	2.0±0.1	2.2±0.1	2.5±0.2
IL-1α (ng/mL)	1.6±0.2	2.7±0.3*	2.0±0.4*
NF_kB (units x 10^{-3})	8.5±4.4	11.0±1.6**	10.7±3.0**

Sources: Campbell et al, Neurotoxicology, 2005; Oberdorster et al., EHP, 2005

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Effects of PM and Traffic on Pulmonary System

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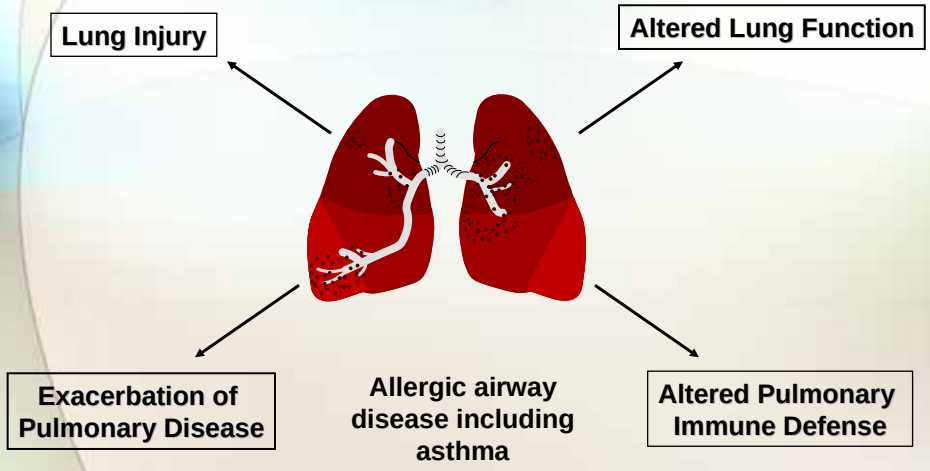
Potential Effects of PM on the Pulmonary System



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Respiratory Health and Traffic

European studies with better estimates of traffic exposure

- Adverse respiratory health associated with exposure to nearby traffic
- Truck traffic (diesel) may be more important
- Effects close to heavy motorways
- Effect may be more prominent in girls

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Traffic-Related Studies

- Cardiopulmonary mortality (Netherlands) and road proximity: 1.95 (1.09-3.52); black smoke: 1.71 (1.10-2.67)
- Wheezing in school children (England): 1.08 (1.00-1.16) (Venn et al, Am J Crit Care Med, 2001) living within 150m of a main road
- Lung function changes in children less than 300 m to freeway (Netherlands): FVC –3.6; FEV1 –4.1(truck traffic density; FVC –2.7; FEV1 –3.7 (black smoke)

Netherlands: Brunekreef and co-investigators

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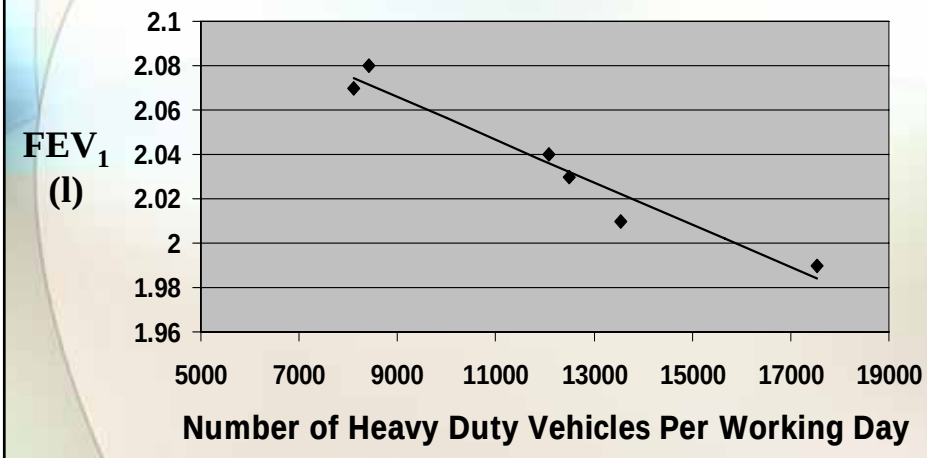
Living within 300m of Major Roadways Affects Lung Function



Source: Brunekreef et al., 1997

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Traffic, Susceptibility and Childhood Asthma

- Asthma and wheeze were strongly associated with residential proximity to a major road (75m from a major road)
- These associations were strongest among children with no parental history of asthma who had lived at the same address since early in life
- In this group, the highest risk occurred adjacent to a major road and risk decreased to background rates at 150-200 m from the road
- Larger risks of asthma associated with long-term residence within 75m of a major road were observed among girls than among boys

Source: McConnell et al., EHP, May, 2006

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Effects of Traffic and PM on Cardiovascular System

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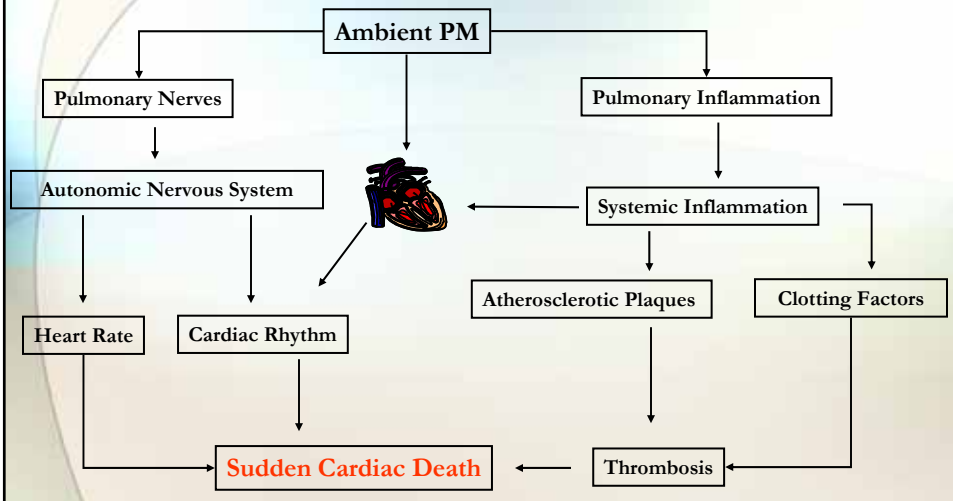
Potential Effects of PM on the Cardiovascular System



Hypothesis: High UFP exposures lead to systemic inflammation through oxidative stress and promote the progression of atherosclerosis?

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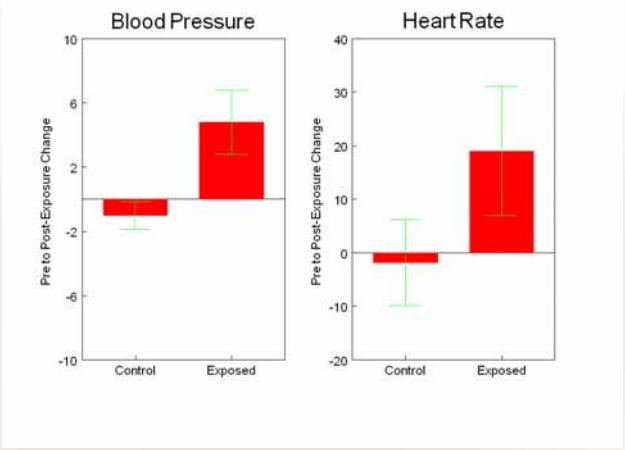
In Vivo Studies--The Geriatric Rat

Blood pressure and heart rate were increased after CAPs exposures



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Panel Studies of Cardiovascular Health

Panel studies with repeated measures show associations between PM and risk of:

- Cardiac ischemia and arrhythmias
- Increased blood pressure
- Decreased heart rate variability
- Increased circulating markers of thrombosis and inflammation

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Ultrafine Studies

- Wichmann et al., 2000: Associations between ambient UFPs and mortality
- Pekankanen et al., 2002: Cardiac ischemia in relation to UF particles. Odds ratio – 2.84 and 10,000 ufp/cm^3
- Chan et al., 2004: Personal exposure to UFP was associated with decreases in heart rate variability- autonomic control of cardiac rhythm associated with increased mortality after MI and related to sudden arrythmic death
- Devlin et al., 2003: Significant decreases in HRV in 10 elderly adults exposed to CAPs from mobile sources

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Traffic Studies – the Heart

- Riediker et al., 2004: Potential physiologic effects of in-vehicle roadside exposures were investigated in North Carolina Highway Patrol troopers
- Findings: markers in the blood, heart beat, decreased lymphocytes, von Willebrand factor, next morning heart beat cycle length, and next morning HRV

"In vehicle exposure may cause pathophysiological changes that involve inflammation, coagulation and cardiac rhythm."

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Exposure to Traffic and the Onset of Myocardial Infarction

Study Intent

- Assess whether exposure to traffic can trigger myocardial infarction

Results

- An association between exposure to traffic and myocardial infarction onset one hour later was observed (odds ratio: 2.9; 95% confidence interval: 2.2 to 3.8, $p<0.001$)
- Time spent in cars, public transport and on bicycles was consistently connected with an increased risk for myocardial infarction

Conclusion

- Transient exposure to traffic might pose a risk in persons vulnerable to myocardial infarctions

Source: Peters et al., NEJM, 2004

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Diesel PM and Cancer

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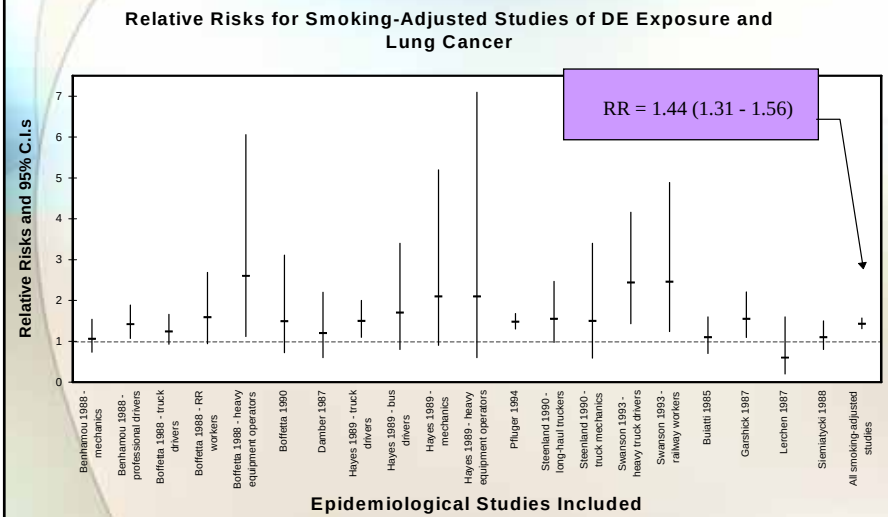
Summary of Diesel Meta-Analysis



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Occupational Diesel Exposure and Lung Cancer

- Garshick et al., EHP, 2004: Lung cancer in railroad workers exposed to diesel exhaust
- Findings: "Our observation of lung cancer risk *[in railroad workers]* is similar to the risk noted by others in the literature. In more than 35 studies of workers with occupational exposure to diesel exhaust, excess risk of lung cancer is consistently elevated by 20–50%."

"These results indicate that **the association between diesel exhaust exposure and lung cancer is real."**

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24-Hour Diesel Particulate Matter Averages (μ g/m³)

	California	Los Angeles
• Average ambient concentration	1.8	2.4
• Average In-vehicle exposure	8.3	12.0

By vehicle and exhaust height (LA):

Tractor-trailer with container	11 μg/m³
Delivery truck, high exh.	14
Delivery truck, low exh.	18
MTA bus, high exhaust	18
MTA bus, low exhaust*	64

*Source: California Air Resources Board

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Comparison on Cancer and Non-Cancer Risks

- Ambient air risk for cancer
  - 7+ excess cancers in 10,000 people.
- Ambient air risk for "acute" cardiovascular mortality:
  - 2+ excess deaths per 1000 people
    (20+ excess deaths per 10,000)

Assuming 2.4 µg/m³ (low estimate)

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Traffic and Reproductive Effects

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Residential Proximity to Freeway Truck Traffic and Preterm & LBW babies

Infants born between 1997-2000 in Los Angeles County

Number of freeway trucks passing within 750 feet of a home per day	Odds Ratio (95% CI)
	(n=4,346; 26,606)
≥ 13,290 trucks	1.23 (1.06-1.43)
≥ 8,684 heavy-duty diesel vehicles	1.18 (1.02-1.37)

Model adjusted for all maternal risk factors as covariates, background air pollution concentrations and census block-group level socio-economic status

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